MYCOSIS FUNGOIDES DEVELOPING IN A PATIENT WITH CONGENITAL ICHTHYOSIFORM ERYTHRODERMA*

Including a Consideration of Multiple Neoplastic Processes

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During the past twenty years we have had under our observation a patient whose clinical course has raised so many questions that her case may be used as a basis for a plan of investigation of the problem of precursors of mycosis fungoides, the nature of mycosis fungoides, and the occurrence of multiple developmental defects and multiple foci of malignant disease. In this patient we have seen during our period of observation a series of seven anaplastic processes, including one congenital ectodermal abnormality and six neoplasms. It is our purpose in this report (1) to present another possible precursor of mycosis fungoides; (2) to emphasize the value of prolonged observation to the understanding of the relationship of one disease process to another, (3) to propose a plan for future investigation of cases of supposed premycosis fungoides, and (4) to suggest possible criteria for the evaluation of cases of so-called mycosis fungoides.

The patient, a Negress, was apparently well until she was seven years of age when an acute episode with chills, fever and coma lasting about twelve hours, was followed by the appearance of red-scaly patches on the face. These gradually spread until the eruption was generalized. Scaling was especially profuse during the winter months. There were no remissions at any time. She had pleurisy at the age of 14 years and penumonia at the age of 15 years. In 1922 (age 32) she had a bilateral salpingo-oöphorectomy because of multilocular right ovarian cyst. In 1924 a fetal abdenoma of the right lobe of the thyroid gland with early hyperplastic goitre was found. In 1927 carcinoma of the uterine cervix was treated by amputation and irradiation. (No recurrence was noted in 1942 and 1945). A diagnosis of congenital ichthyosiform erythroderma of Brocq (ichthyosiform hyperkeratosis) was made in 1924 (1), and the diagnosis was confirmed when the patient was seen at the Hospital of the University of Pennsylvania in 1925 and 1929. In 1925 a 12-pound uterine tumor was removed. On April 15, 1941, she returned because of verrucoid hyperkeratotic patches on the extremities and an indurated ulcerative lesion adjacent to the left angle of the mouth (Figures 1, 2). This was associated with local adenopathy and had appeared during the previous two years. Similar ulcerative tumor masses had also appeared on the chin, the upper lip, the forehead and the medial aspect of the left thigh. The lip and chin lesions were painful. The patient complained of marked fatigue.

Histologic examination of the skin taken from the left thigh on 4-23-41 (Figure 3) showed scanty parakeratosis, edema and elongation and broadening of the interpapillary pegs. There was slight migration of cellular infiltrate into the epidermis; questionable Pautrier's abscesses; edema of the papillae with vascular dilatation and a scanty infiltration of cells of fairly uniform type. There were

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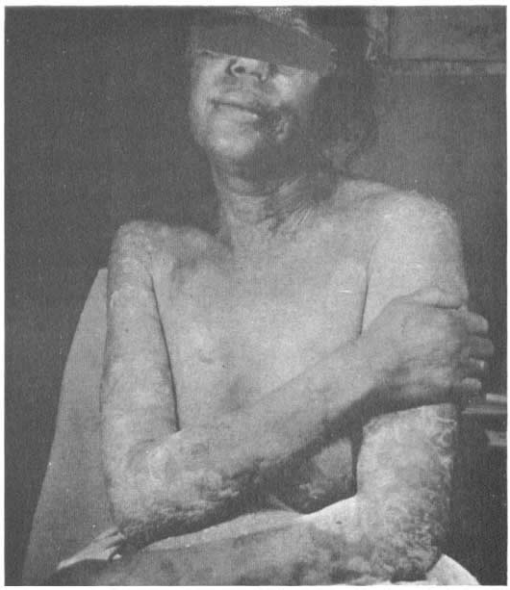

FIG. 1. FRONT VIEW OF PATIENT SHOWING LESION LEFT SIDE OF MOUTH, NECK, SHOULDERS, ARMS AND FOREARMS

FIG. 2. CLOSE-UP OF HYPERKERATOTIC LESIONS ON FOREARM

some chromatophores. A section taken from a verrucous lesion on the left thigh at the same time showed essentially the same features except for marked accumulation (Figure 4) of hyperkeratotic material in crypts. The epiderm was less

thickened and the interpapillary pegs were extremely wide. These sections, although not definitely typical, were considered to be compatible with mycosis fungoides. On 8-27-41 a section from a lesion of the left side of the face about the angle of the mouth revealed marked pseudoepitheliomatous hyperplasia near the margin of the ulcerated surface and a multiplicity of cell types in the corium. At this time the histologic features were those of mycosis fungoides.

The patient was hospitalized from 4-21-41 to 5-17-41. Investigation of the ears, nose and throat, gynecologic study, a roentgenogram of the chest and fractional gastric analysis,

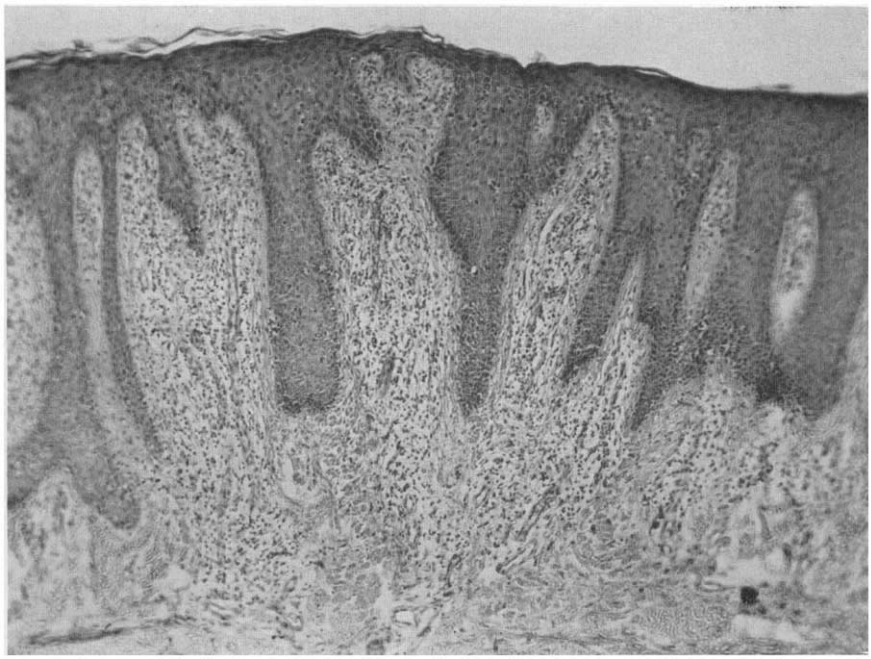

FIG. 3. ×110 BIOPSY SPECIMEN TAKEN FROM LEFT THIGH IN 1941. ACANTHOSIS, VASCULAR DILITATION AND CELLULAR INFILTRATE SUGGEST MYCOSIS FUNGOIDES

revealed normal conditions. Serologic tests for syphilis elicited negative reactions. The basal metabolic rate was plus 9 per cent. The sedimentation rate was moderately increased.

A dental roentgenogram revealed several carious teeth, which were extracted. Sternal biopsy showed overactive bone marrow but normal leukopoiesis and erythropoiesis and a slightly increased eosinophile count. The total cholesterol content of blood was 250 milligrams and the free cholesterol content 175 milligrams per 100 cubic centimeters. Values for blood sugar, blood urea nitrogen and serum protein were normal. The hemoglobin content ranged from 65 to 85 per cent; there were 4,600 leukocytes, of which 54 per cent were polymorphonuclear leukocytes, 11 per cent monocytes, 30 per cent lymphocytes, and 5 per cent eosinophiles. Urinalysis did not reveal the presence of iodides or bromides and arsenic determination in the skin and urine gave negative results. Cultures on Sabouraud's medium produced a growth of Monilia and cultures of skin disclosed aerobic hemolytic streptococcii, many anaerobic hemolytic streptotocci, Bacillus proteus and hemolytic Staphylococcus aureus.

The nodulo-ulcerative lesions of the right thigh were treated by roentgen irradiation by means of the Chaoul technic. A total of 2900r was given, the following factors being used: 50 kilovolts; 1 mm. aluminum and 0.5 mm. copper filter;

FIG. 4. ×110 BIOPSY SPECIMEN TAKEN IN 1941 FROM HYPERKERATOTIC LESIONS. SAME FEATURES AS FIGURE 3 PLUS HYPERKERATOTIC MATERIAL IN CRYPT

25 cm. skin target distance. The lesions of the chin and forehead were similarly treated. Other therapy included intramuscualr liver extract, ointments, sulfadiazine orally and administration of Vitamin A and B_1 (thiamine hydrochloride).

The patient was presented before the Philadelphia Dermatological Society in 1941 (2) as mycosis fungoides versus congenital ichthyosiform erythroderma. At that time the diagnosis of congenital ichthyosiform erythroderma was re-

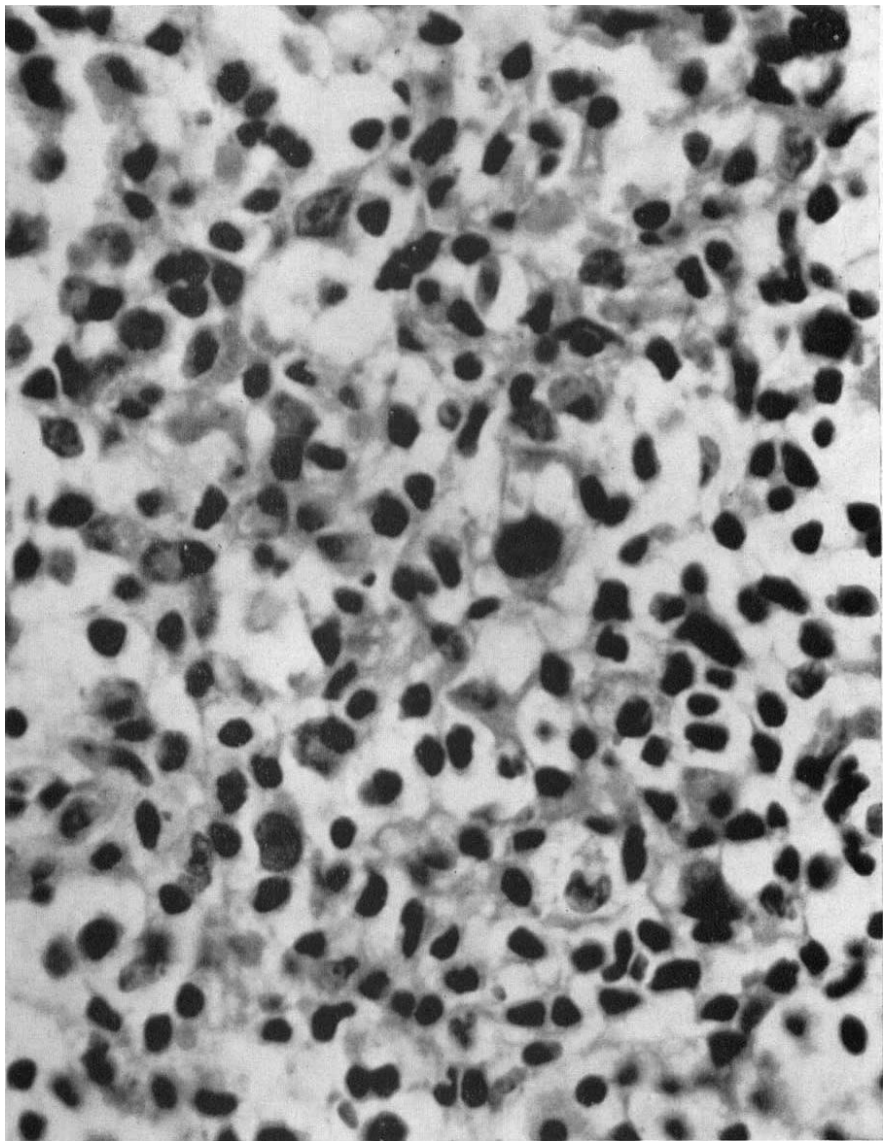

FIG. 5. HIGH-POWER VIEW OF POLYMORPHIC INFILTRATE IN LESION FROM FOREHEAD ×1012

affirmed by Dr. Greenbaum who stated that in 1924 the lesions were scaly and red as at this time, but not as infiltrated. Dr. Shaffer agreed with Dr. Greenbaum since he, too, had seen the patient several years before. It was not settled

whether the congenital ichthyosiform erythroderma from the beginning was premycosis fungoides, since unfortunately, no biopsy specimen had been taken during the congenital ichthyosiform erythroderma phase of the process. A biopsy at the presentation in 1941 from the forehead lesion showed pseudoepitheliomatous hyperplasia and a multiform type of infiltrate in the corium with a large number of eosinophiles (Figure 5). In March 1942, roentgenogram of the chest, the skull and jaw yielded normal findings. The patient was presented again to the Philadelphia Dermatological Society on 3-20-43 (3) as mycosis fungoides (relationship to congenital ichthyosiform erythroderma). At that time Dr. Garner, who had seen the patient in 1929, confirmed his previous diagnosis of congenital ichthyosiform erythroderma, but felt that the newly developed infiltrations were definitely those of mycosis fungoides.

On October 28, 1943, the patient reported to the Medical Department complaining of diarrhea and loss of weight. On 12-2-43 a diagnosis of carcinoma of the rectum was made. Proctologic examination showed adeno-carcinoma con-

1922—Multiocular right ovarian cyst. Bilateral salpingo-oöphorectomy.
1924-25—Fetal adenoma right lobe of thyroid gland with early hyperplastic toxic goitre.
Congenital ichthyosiform erythroderma (Greenbaum and Schamberg)
1925—Twelve-pound uterine tumor removed.
1927—Carcinoma of cervix. Treated by amputation and irradiation (No recurrence, 1942 and 1945).
1929—Congenital ichthyosiform erythroderma (Dermatological Service).
1936-1941-1939, Mycosis fungoides. 1941, Sternal marrow biopsy normal. Nodules on face and thigh; mycosis fungoides; irradiated.
1944—Adenocarcinoma of the rectum resected. *Metastases to lung, liver and regional lymph nodes.* Inguinal node showed reticulum hyperplasia.
1945—Death—multiple metastasis (autopsy) October 1945.

FIG. 6. SUMMARY OF CLINICAL COURSE

sisting at 10 cms. of a large, easily bleeding, fungating cauliflower-like growth arising from the posterior rectal wall. On 1-2-44 an abdomino-perineal resection was done and a large locally extending carcinoma with extension to the perirectal lymphnodes was removed. On 4-7-45 the patient was admitted to the medical ward with the complaint of swelling of the legs, especially at night. Biopsy specimen from enlarged inguinal lymphnodes showed proliferative endotheliosis, but no carcinoma cells. Roentgenogram of the lung revealed changes interpreted as metastatic infiltration. In September 1945 the patient had developed dyspnea, cough, weakness and anorexia, and was admitted on 10-11-45. Examination revealed a rather ill patient with palpable inguinal lymphnodes, generalized ichthyosiform scaly eruption, fluid in both lung bases, friction rub in the left chest, an enlarged heart, palpable liver, ascites and edema of the abdominal wall. Roentgenogram of the chest on 10-16-45 confirmed the presence of metastatic lesions in the right and left lung fields. There was an opacity in the lower left lung field, probably due to pleural effusion. The patient died 10-19-45 of cardiac failure.

The autopsy was performed by Dr. William Weiss, Jr. and revealed bilateral

pleural effusion, metastatic carcinoma of both lungs, liver and various lymphmodes.

Histologically the skin showed chronic dermatitis with hyperplasia of epithelium; acute and chronic inflammation of scalp with ulceration. Dr. Weidman, who also reviewed the sections of skin taken at autopsy, felt that none of the characteristics of mycosis fungoides were present. They presented only chronic inflammatory changes, probably due to response to roentgen irradiation.

CONGENITAL ICHTHYOSIFORM ERYTHRODERMA AS PRECURSOR OF MYCOSIS FUNGOIDES

Nowhere have we found mention of congenital ichthyosiform erythroderma as a precursor of mycosis fungoides. Although erythrodermas of long standing have been rated as the most common type of premycotic lesion, none of the cases reported fit into the category of congenital ichthyosiform erythroderma (4, 5, 6, 7, 8). Various so-called established clinical entities have been shown to be premycotic processes. Keil and others (9, 10, 11, 12) (denied by Montgomery and Burkhart (13)) have demonstrated this for parapsoriasis en plaques disseminées of Brocq, and Oliver (14) as well as Dostrovsky and Sagher (15) for poikiloderma. The frequency with which certain forms of parapsoriasis or poikilodermatic states may terminate as mycosis fungoides is unsettled. Since congenital ichthyosiform erythroderma is rare in the first place, it cannot be a common premycotic lesion. However, if one concedes that congenital ichtyhosiform erythroderma may be a premycotic phase of mycosis fungoides, there are many questions still unanswered as to the exact relationship of the two processes. (1) Will all patients with congenital ichthyosiform erythroderma eventually develop mycosis fungoides, if followed long enough? (2) Are the two diseases separate entities but based on the same constitutional background? (3) Does the presence of congenital ichthyosiform erythroderma lead to increased susceptibility to mycosis fungoides? Because of the rarity of congenital ichthyosiform erythroderma, these questions cannot be answered as easily for the present circumstances as they night be for the relationship between mycosis fungoides and poikilodermatic states and certain forms of parapsoriasis and other erythrodermas.

Insofar as favorable response to irradiation has been used as a differential criterion in distinguishing premycotic mycosis fungoides from parapsoriasis en plaques, the criterion could also be applied to congenital ichthyosiform erythroderma. As is the case with parapsoriasis, congenital ichthyosiform erythroderma is resistant to all forms of treatment. Therefore, failure of an eruption of this character to clear does not eliminate the possibility of mycosis fungoides. On the other hand, outright examples of mycosis fungoides have been notoriously resistant to both roentgen irradiation and arsenical therapy (16) and congenital ichthyosiform erythroderma may, as in our case, undergo seasonal changes.

Not all cases of undoubted premycosis fungoides lesions reach the stage of tumor formation, especially if the period of observation is too brief. The presence of banal histologic changes in a lesion does not eliminate the possibility

of subsequent development of mycosis fungoides. Therefore, since the group of premycotic lesions comprises such a wide variety of clinically distinctive types, we do not feel it is unreasonable to add congenital ichthyosiform erythroderma to the list.

If it is not conceded that our patient represents an example of mutation of congenital ichthyosiform erythroderma to mycosis fungoides, but that the scaling eruption represents the premycotic phase of disease, it is still distinguished by the long duration of the premycotic phase—49 years. The average median duration of this phase of mycosis fungoides is 4.5 years with a range of five to seven years (17). In Keil's (9) excellent presentation of the subject of parapsoriasis en plaques disseminées, and incipient mycosis fungoides, he cited cases from the literature in which the eruption lasted from 20 to 50 years. Accordingly, the long duration of the eruption in our patient does not preclude it as a true example of premycotic mycosis fungoides. It also emphasizes the importance of long observation of all scaly erythrodermas to determine whether they terminate as mycosisfungoides. As was suggested by Besnier (18), "In the presence of achronic, ambiguous pruritic dermatitis, rebellious to ordinary treatment and which assumes the form of a vague erythroderma, of a psoriasis, of an eczema, of a rebellious urticaria, of a lichenoid prurigo, etc., it is necessary to bear in mind the question of a possible mycosis fungoides."

MULTIPLE PRIMARY MALIGNANT TUMORS

The problem of multiple primary malignant tumors has been surveyed in the monumental study of Warren and Gates (19). No case like ours was noted by these investigators, nor did they offer a satisfactory explanation, beyond so-called predisposition or susceptibility, to account for multiple tumors. It is interesting that two to four percent of all tumor patients are found to have multiple primary malignant tumors (two or more) of the same or different embryonal origin. The question whether the presence of one primary focus of cancer prevents or predisposes to another focus of malignancy has been the subject of much speculation. Although there are some (Peller and Stephenson) who believe that the intentional production of curable cutaneous cancer by irritations which are not carcinogenic to internal organs may prevent cancer of internal organs, others (Warren and his colleagues, et al.) cite convincing evidence that this is not always the case. On the contrary, cancer of the skin is more frequently associated with multiple cancer than would be expected on the basis of chance alone. We cannot offer a real explanation for this finding which, however, does *suggest* the necessity of a complete survey of every patient presenting an established malignant lesion (e.g. of the skin) for other foci of neoplastic change (e.g. gastrointestinal tract; genito-urinary tract, etc.). This is merely emphasis of the dictum that a person with one embryonal or developmental defect, is likely to possess others.

In our case the successive occurrence of seemingly independent foci of carcinoma (cervix and rectum) raises the question of whether previous irradiation of the cervix may have induced the rectal lesion. We have no evidence either for or against this possibility.

NOSOLOGY OF MYCOSIS FUNGOIDES

The exact nosologic position of mycosis fungoides is still far from settled. Not only is there no real unanimity as to a suitable name for the process, but as time goes on, more and more cases are separated from it as greater knowledge has accumulated regarding their histopathology. To add to the confusion, some clinical cases terminate as leukemia; others may present a variety of clinical and pathologic pictures at times resembling Hodgkin's disease, or leukemia or lymphosarcoma; or there may be features indicative of several at once. The usual non-characteristic clinical and histologic picture of the early premycotic phase, which may last for months or years, does not serve to simplify the situation.

Fraser in 1917 (20) stated that mycosis fungoides can be explained by one of nine views: (Granuloma, cutaneous form of lymphadenoma, lymphosarcoma, a condition midway between a granuloma and sarcoma, alymphemic lymphomatosis, sarcoma engrafted on a previous dermatosis (psoriasis or eczema), last phase of a series of dermatoses that include pityriasis rosea and parapsoriasis, lymphoma of the skin, and cutaneous manifestations of systemic disease). While many believe mycosis fungoides a specific disease *sui generis*, Symmers (21) thought mycosis fungoides was not a clinical or pathologic entity. Gates concurs in this view.

Various writers of recent years have considered mycosis fungoides as a lymphoblastoma (with mutation) (22, 23); a disorder of the reticulo-endothelial system (24, 25, 26, 27, 28): sarcoma (29, 30, 31, 32); a skin disease *sui generis* (27, 28, 33); and a visceral disease of a specific nature (neoplastic) often extending to lymph-nodes and internal organs. This last view has a large number of supporters (34, 35, 36, 37, 38, 39, 40, 41, 42). Robb-Smith (43) in 1944 stated that "through all the varying accounts one gains the impression there is a distinct clinical entity with a characteristic histology, and that if really critical observation and histology were applied to these disorders (reticuloses) mycosis fungoides would stand out even more certainly as a disease with a characteristic natural history and pathology."

In none of the reported cases of histologic mycosis fungoides have the infiltrations (metastases) of the internal organs been epithelial. On the other hand, multiple lesions of the skin clinically resembling mycosis fungoides and varying from areas of simple erythema to tumors were reported by Ketron and Goodman (44). The pathologic process was caused by a malignant proliferation of epidermal structures that did not resemble the usual or atypical histologic changes reported in mycosis fungoides. A similar case was reported by Schmidt (45). This case, however, was later studied by Beeson and Hueper (46), who at autopsy made the diagnosis of sarcomatosis of the skin. Goeckerman and Montgomery (47) also reported a case in which on histologic grounds, the question was raised whether the so-called mycosis fungoides was a malignant epithelial neoplasm rather than a lymphoblastoma. Montgomery (48) stated that he had seen two additional cases about which there has been a difference of opinion among pathologists. Montgomery's interpretation is that these cases represent malignant

invasion of the epidermis by cells of the lymphocytic series, rather than that the cells of the infiltrate are altered epithelial cells. He rules out any possibility of relationship of epithelial tumors to mycosis fungoides.

ASSOCIATION OF VARIOUS DISEASES WITH MYCOSIS FUNGOIDES

Careful search of the literature has revealed that only rarely is mycosis fungoides simultaneously associated with other diseases. Mycosis fungoides has been seen in association with Mikulicz's disease (49), lupus erythematosus (50, 51), hemorrhagic sarcoma of Kaposi (52), psoriasis; and tuberculosis (53). The only recent example of mycosis fungoides in a patient with carcinoma of the intestinal tract which we have been able to find is that of Skeer (54). This patient was a 58-year-old Russian-born woman who had an eruption of the breasts of three months' duration (histologically mycosis fungoides), diabetes mellitus, generalized arteriosclerosis, bloody stools and cramps of six weeks' duration in 1942. Examination revealed carcinoma of the sigmoid near the splenic flexure with intususception. The resected portion of the tumor revealed adenocarcinoma. The commentators and presentor indicated that there was no apparent connection between the carcinoma and the mycosis fungoides. In a careful study of 546 cases of mycosis fungoides in the literature, Jordan and Areschewa (55) found that death usually occurred after a prolonged cachectic state. Among 136 cases from the literature and the authors' own experience, they found 38 cases which terminated fatally. Death was due to cachexia in 10; probable roentgen ray damage in 10; metastases to internal organs in 4; lung, heart, brain or endocrine gland complications in 5; intercurrent disease in 1; unstated causes in 8. It is noteworthy that in none was there evidence that carcinoma was the cause of the fatal termination.

MYCOSIS FUNGOIDES IN THE NEGRO

Mycosis fungoides is said to be rare in the Negro. This view is concurred in by various of the older writers as well as by many recent observers (56, 57, 58). In his review of this subject Sigel (58) could find no special clinical or histological differences between mycosis fungoides in white and in Negro patients.

We have seen one other Negro with mycosis fungoides recently on our service. While the disease is uncommon in the Negro, the race of the patient is of no help in assaying the pathogenesis of our cases.

SUGGESTED PROGRAM FOR STUDY OF FUTURE CASES

Because future events in a patient's clinical course cannot be foreseen, a number of procedures are suggested which would have helped to clarify some aspects of the complex situation our patient presents. These suggestions are offered as being useful in the investigation of similar cases. By means of carefully collected and correlated material, advances and even experimental approaches to the problems presented in this report may be developed. Although most of these suggestions are the fundamentals of rational practice, and have been individually proposed and advised by many investigators, especially Wayson and Weidman

(59); Custer (60); Keil (61); Mercer (62); and Loveman (63), we make no apology for listing them here:

1. Careful, detailed records of all clinical events.
2. Repeated biopsy studies at intervals in *all* dermatoses of obscure character or long duration or of unusual resistance to therapy.
3. Prolonged follow-up observation even after apparent and unexpected "cure" or improvement.
4. Careful roentgenographic studies (pulmonary, gastro-intestinal, renal, bone).
5. Repeated general medical and special examinations.
6. Hematologic study by accepted methods, including repeated cytologic investigations of blood, bone marrow and lymphnodes. These would include the oxidase test, special connective tissue stains, and study of the bone marrow by the trephine method (60) which preserves the form and relationship of the bone marrow cells, and, if possible, lymphnode and other impressions (skin) (64), and autopsy study of the liver and spleen.
7. Tissue culture.
8. Application of new investigative methods from any field of medicine to this problem.
9. Central registry of a suitable center of all such obscure dermatological (61) (43) cases. Correlation of the data in this center with related centers in other field (e.g. tumor registry, etc.).

SUMMARY AND CONCLUSIONS

1. A patient is presented in whom during a period of over 20 years there occurred a series of 7 neoplastic and ectodermal abnormalities: ovarian cyst; fetal adenoma of the thyroid; congenital ichthyosiform erythroderma; uterine tumor; carcinoma of the uterine cervix; mycosis fungoides; and adenocarcinoma of the rectum.

2. Congenital ichthyosiform erythroderma is proposed as a possible precursor of mycosis fungoides.

3. Mycosis fungoides is discussed from the standpoint of its relationship to ectodermal tumors; its occurrence in the Negro, and duration of the pre-mycotic phase.

4. A list of desirable procedures for the investigation of such complex cases is presented. This includes, among others, the proposal of a central clearing house for such rare cases.

BIBLIOGRAPHY

1. Greenbaum, S. S. and Schamberg, J. F.: Ichthyosiform Hyperkeratosis. Arch. Dermat. and Syph., **11**: 555, 1925.
2. Beerman, H. and Tavs, L. E.: Case for Diagnosis (Mycosis Fungoides ?), Congenital Ichthyosiform Erythroderma ?). Arch. Dermat. and Syph., **44**: 1168, 1941.
3. Beerman, H. and Tavs, L. E.: Mycosis Fungoides (Relationship to Congenital Ichthyosiform Erythroderma). Arch. Dermat. and Syph., **49**: 366, 1944.
4. MacKee, G. M. and Rosen, I.: Erythroderma Congelitale Ichthyosiforme. J. Cutan. Dis., **35**: 235–252, 343–361, and 511–540, 1917.

5. WILE, J. J.: Familial Study of Three Unusual Cases of Congenital Ichthyosiform Erythroderma. Arch. Dermat. and Syph., **10:** 487–498, 1924.
6. WEISS, R. J. AND TOBIAS, N.: XLII—Congenital Ichthyosiform Erythroderma, Arch. Dermat. and Syph., **12:** 182–194, 1925.
7. GOECKERMAN, W. H.: Bullous Ichthyosiform Erythroderma, Arch. Dermat. and Syph., **14:** 158–172, 1926.
8. LAWLESS, T. K.: Congenital Ichthyosiform Erythroderma, Arch. Dermat. and Syph., **44:** 30–36, 1941.
9. KEIL, H.: Parapsoriasis en Plaques Disseminées and Incipient Mycosis Fungoides: A Critical Review with a Report of an Illustrative Case, Arch. Dermat. and Syph., **37:** 465–494, 1938.
10. KEIL, H.: Parapsoriasis en Plaques Disseminées and Incipient Mycosis Fungoides: Supplementary Data in Their Development, Arch. Dermat. and Syph., **38:** 545–554, 1938.
11. MCCARTHY, L.: Differential Diagnosis of Parapsoriasis, Arch. Dermat. and Syph., **45:** 81–102, 1942.
12. ABRAMOWITZ, E. W. AND KANEE, B.: Mycosis Fungoides: Two Unusual Types, One Presenting Leonine Facies; the Other, Parapsoriasis (?) in Patches for Thirty Years, N. Y. State J. Med., **45:** 512–518, 1945.
13. MONTGOMERY, H. AND BURKHART, R. J.: Parapsoriasis: Its Relation to Mycosis Fungoides and Tuberculosis, Arch. Dermat. and Syph., **46:** 673–690, 1942.
14. OLIVER, E. A.: Mycosis Fungoides with Poikiloderma-like Symptoms, Arch. Dermat. and Syph., **33:** 267–289, 1936.
15. DOSTROVSKY, A. AND SAGHER, F.: Poikiloderma as the Initial Stage of Mycosis Fungoides, Arch. Dermat. and Syph., **51:** 182–188, 1945.
16. GARB, J. AND WISE, F.: Mycosis Fungoides with Bullous Lesions, Arch. Dermat. and Syph., **48:** 359–368, 1943.
17. GATES, O.: Cutaneous Tumors in Leukemia and Lymphoma, Arch. Dermat. and Syph., **37:** 1015–1030, 1938.
18. BESNIER, cited by ORMSBY, O. S. AND MONTGOMERY, H.: Diseases of the Skin. Lea and Febiger, Philadelphia, 1943.
19. WARREN, S. AND GATES, O.: Multiple Primary Malignant Tumors. A Survey of the Literature and Statistical Study. Am. J. Cancer, **16:** 1358–1414, 1932.
20. FRASER, J. F.: The Pathology of Mycosis Fungoides, J. Cutan. Dis., **35:** 793, 1917.
21. SYMMERS, D.: Mycosis Fungoides as a Clinical and Pathologic Nonexistent, Arch. Dermat. and Syph., **25:** 1–5, 1932.
22. WILE, U. J. AND STILES, F., JR.: Clinical Mutations in Lymphoblastomas, J. A. M. A., **104:** 532–536, 1935.
23. MONTOGMERY, H. AND WATKINS, C. H.: (a) Monocytic Leukemia; Cutaneous Manifestations of the Naegeli and Schilling Types; Hemocytologic Differentiation, Arch. Int. Med., **60:** 51–63, 1937; (b) Exfoliative Dermatitis as a Manifestation of Monocytic Leukemia (Schilling), Proc. Staff Meet. Mayo Clin., **13:** 294–297, 1938.
24. GRYNFELTT, E., MARGAROT, J. AND RIMBAUD, P.: Remarques sur l'histogénèse et sur l'étiologie du mycosis fongoïde, Bull. Soc. franç. de Dermat. et Syph., **44:** 1389–1394, 1937.
25. COTTINI, G. B.: Aspects hematologiques et histopathologiques de trois cas de mycosis fongoïde, Ann. de dermat. et syph., **8:** 15–44, 1937.
26. BERGER, L. AND VALLÉE, A.: Le mycosis fongoïde: une réticuloendotheliose de la peau, Presse Méd., **38:** 177–179, 1930.
27. ZOON, J. J.: Notes diagnostiques et thérapeutiques au sujet du mycosis fongoïde, Bull. Soc. franç. de dermat. et syph., **44:** 1282–1290, 1937.
28. JAFFÉ, R. H.: The Reticulo-Endothelial System in Downey, H. Handbook of Hematology, New York, B. Hober, Inc., 1938, Vol. 2, pp. 1105–1107.
29. FRASER, J. F.: (a) Mycosis Fungoides; Its Relation to Leukemia and Lymphosarcoma,

Arch. Dermat. and Syph., **12:** 814–827, 1925; (b) The Interpretation of Mycosis Fungoides as a Variety of Lymphosarcoma, Ibid., **11:** 425–445, 1925.

30. KEIM, H. L.: The Lumphoblastomas: Their Interrelationships, Arch. Dermat. and Syph., **19:** 553–594, 1924.
31. MAYR, J. K.: (a) Zur Klinik und Histologie der Mycosis Fungoides d'emblée, Dermat. Ztschr., **33:** 185, 1921; (b) Zur Klinik und Histologie der Mycosis Fungoides, Arch. f. Dermat. u. Syph., **145:** 306, 1924.
32. HEMMINGSON, H.: Ein Fall von Mycosis Fungoides mit Metastasierung als polymorphzelliges Sarkom, Acta Radiol., **22:** 606–619, 1941.
33. ORMSBY, O. S. AND FINNERUD, C. W.: Mycosis Fungoides; Report of a Case with Autopsy, Arch. Dermat. and Syph., **27:** 631–642, 1933.
34. SEQUIERA, J. H.: Proc. Roy. Soc. Med. Derm. Sect., **7:** 190, 1913–14.
35. PAULTAUF, cited by LIECHTI, E.: No. 42.
36. BENNEK, J.: Mycosis fungoides innerer Organe. Zbl. Haut. u. Geschlichskr, **60:** 1–21, 1938.
37. BERMAN, L.: Pathologic Nature of Mycosis Fungoides, Arch. Path., **29:** 530–540, 1940.
38. (a) PAUTRIER, L. M., HOERNER, G. AND WORINGER, F.: Résultats fournis par l'autopsie du cas de mycosis fongoïde avec tumeurs, presenté à la seance de mars dermier, Bull. Soc. franç. de Dermat. et Syph., **47:** 8–14, 1940; (b) PAUTRIER, L. M., Un nouveau type de granulomatose en tumeurs generalisées, simulant le mycosis fongoïde à évolution mortelle, Dermatologica, **87:** 190, 1943; (c) PAUTRIER, L. M. AND WORINGER, F.: Tumeurs récidivantes de la jambe droite, évolutant par poussées depuis trois ans, ayant presenté initialement une histologie de lymphosarcome et paraissant aller vers un mycosis fongoïde en tumeurs, Bull. Soc. franç. de Dermat. et Syph., **45:** 1909, 1935.
39. GADRAT, J.: A propos d'un cas de mycosis fongoïde avec autopsie; considerations sur l'histogénèse comparée au mycosis fongoïde, et de la lymphogranulomatose, Ann. de Dermat. et Syph. **10:** 398–409, 1939.
40. MACCORMAC, H.: Mycosis Fungoides Treated By Malaria, Terminating in Hodgkin's Disease, Brit. Med. J., **2:** 645–646, 1941.
41. GOLDSMITH, W. N.: The Reticuloses, Brit. J. Dermat. and Syph., **56:** 107–128, 1944.
42. LIECHTI, E.: Uber Tumoren innerer Organe bei Mycosis Fungoides, Arch. f. Dermat. u. Syph., **154:** 246–268, 1928.
43. ROBB-SMITH, A. H. T.: The Reticular Tissue and the Skin, Brit. J. Dermat. and Syph., **56:** 151–176, 1944.
44. KETRON, L. H. AND GOODMAN, M. H.: Multiple Lesions of the Skin Apparently of Epithelial Origin Resembling Clinically Mycosis Fungoides, Arch. Dermat. and Syph., **24:** 758–785, 1931.
45. SCHMIDT, F. R.: Multiple Tumors of the Skin Resembling Mycosis Fungoides, Arch. Dermat. and Syph., **18:** 231, 1938.
46. HUEPER, W. C. AND BEESON, B. B.: Primary Multiple Sarcomatosis of the Skin, Arch. Dermat. and Syph., **19:** 794–799, 1929.
47. GOECKERMAN, W. H. AND MONTGOMERY, H.: Cutaneous Lymphoblastoma, Arch. Dermat. and Syph., **24:** 385–395, 1931.
48. MONTGOMERY, H.: Exfoliative Dermatosis and Malignant Erythroderma; the Value and Limitations of Histopathologic Studies, Arch. Dermat. and Syph., **25:** 8–23, 1935.
49. THRONE: Mycosis Fungoides and Mukulicz's Disease, Arch. Dermat. and Syph., **16:** 812, 1927.
50. FEIT: Lupus Erythematosus and Mycosis Fungoides, Arch. Dermat. and Syph., **21:** 478, 1930.
51. HALLOPEAU, cited by FEIT: No. 50.
52. LANE, C. G. AND GREENWOOD, A. M.: Lymphoblastoma (Mycosis Fungoides) and Hemorrhagic Sarcoma of Kaposi in the Same Person. Arch. Dermat. and Syph., **27:** 643–654, 1933.

53. CANNON, A. B.: Mycosis Fungoides, Pulmonary Tuberculosis, Arch. Dermat. and Syph., **46:** 330, 1942.
54. SKEER, J.: Mycosis Fungoides in a Patient with Carcinoma of the Colon, Arch. Dermat. and Syph., **47:** 860, 1943.
55. JORDAN, A. AND ARESCHEWA, W.: Das Schicksal der Kranken mit Mycosis fungoides (M.f.), Dermat. Ztschr., **74:** 126–135, 1936.
56. FOX, H.: Observations on Skin Diseases in the Negro, J. Cutan. Dis., **26:** 67–79 and 109–121, 1908.
57. STROBEL, E. R. AND HAZEN, H. H.: Mycosis Fungoides in the Negro, J. Cutan. Dis., **29:** 147, 1911.
58. SIGEL, H.: Mycosis Fungoides in the Negro, Arch. Dermat. and Syph., **52:** 18–20, 1945.
59. WAYSON, J. T. AND WEIDMAN, F. D.: Aleukemic Reticulosis, an Additional Member of the Group of So-Called Cutaneous Lymphoblastomas, Arch. Dermat. and Syph., **34:** 755–774, 1936.
60. CUSTER, R. P.: Studies on the Structure and Function of Bone Marrow, Am. J. Med. Sci., **185:** 617, 1933. Chapter 41, pps. 500–521, The Bone Marrow in Kracke, R. R., Diseases of the Blood, an Atlas of Hematology, J. B. Lippincott Co., Philadelphia, 1941, Second Edition.
61. KEIL, H.: Correspondence, Brit. J. Dermat. and Syph., **51:** 48, 1939.
62. LOVEMAN, A. B.: Monocytic Leukemia Cutis, South. M. J., **29:** 357, 1936.
63. MERCER, S. T.: The Dermatosis of Monocytic Leukemia, Arch. Dermat. and Syph., **31:** 615–635, 1935.
64. SWEITZER, S. E. AND WINER, L. H.: Ulcerative Hodgkin's Disease and Lymph Node Imprints, Arch. Dermat. and Syph., **51:** 229–236, 1945.